Patent Claims

1. Method for the identification of cytosine methylation patterns in genomic DNA samples characterized in that:

a) a genomic DNA sample is treated chemically in such a way that cytosine and 5-methylcytosine react differently and a different base pairing behavior of the two products is obtained in the duplex;

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b) portions of the thus-treated DNA sample are enzymatically amplified;

c) the amplified portions of the thus-treated DNA sample are bound to a surface;

d) a set of probes of different nucleobase sequences, each of which contains the dinucleotide sequence 5'-CpG-3' at least once, are hybridized to the immobilized DNA samples;

e) the non-hybridized probes are separated;

f) the hybridized probes are analyzed in a mass spectrometer, wherein the position of the probes on the sample holder permits a classification of the hybridizing DNA sample;

g) assignment of the peak pattern obtained from the mass spectra to the methylation pattern and comparison of the new data with a database.

2. Method according to claim 1, further characterized in that one or more amplified genomic DNA fragments are immobilized in c) by hybridization

with complementary oligonucleotide or PNA sequences, which are covalently bound to the surface.

3. Method according to claim 2, further characterized in that a cross-linking of the genomic DNA fragments with the oligonucleotide or PNA sequences bound to the surface results after the hybridization.

4. Method according to claim 3, further characterized in that covalent chemical bonds are formed for the cross-linking.

5. Method according to claim 3, further characterized in that electrostatic interactions are formed for the cross-linking.

6. Method according to one of claims 3 to 5, further characterized in that the oligonucleotide or PNA sequences bound to the surface contain 5-bromouracil structural units.

7. Method according to at least one of the preceding claims, further characterized in that the immobilized complementary oligonucleotide sequences contain modified bases, ribose or backbone units.

8. Method according to one of the preceding claims, further characterized in that the genomic DNA sample is propagated in b) in the form of several amplified fragments, so that at least 0.01% of the total genome is amplified.

9. Method according to at least one of the preceding claims, further characterized in that the mixture of amplified DNA fragments is bound to a surface, on which a multiple number of different points is arranged, each of which can bind different portions of the amplified DNA sample.

10. Method according to one of the preceding claims, further characterized in that a set of probes is used in d), which contains the dinucleotide sequence 5'-CpG-3' only once in each probe and the probes otherwise contain either no cytosine or no guanine bases.

11. Method according to one of the preceding claims, further characterized in that a bisulfite or pyrosulfite or disulfite solution or a mixture of the indicated solutions is used together with other reagents for the specific or sufficiently selective conversion of cytosine to uracil.

12. Method according to one of the preceding claims, further characterized in that the surface used for the immobilization of amplified sample DNA is also the sample holder for a mass spectrometer.

13. Method according to at least one of claims 1 to 11, further characterized in that the surface used for the immobilization of amplified sample DNA is introduced as a whole, prior to f), onto a sample holder for a mass spectrometer.

14. Method according to one of claims 1 to 13, further characterized in that the hybridized probes are stripped from the immobilized amplified DNA samples before, after or by contact with a matrix.

15. Method according to one of the preceding claims, further characterized in that the probes are nucleic acids, which bear one or more mass tags.

16. Method according to claim 15, further characterized in that one or more mass tags are also charge tags.

17. Method according to claim 15, further characterized in that the probes also bear a charge tag.

18. Method according to one of the preceding claims, further characterized in that the probes are modified nucleic acid molecules.

19. Method according to claim 20, further characterized in that the modified nucleic acid molecules are PNAs, alkylated phosphorothioate nucleic acids or alkyl phosphonate nucleic acids.

20. Method according to one of the preceding claims, further characterized in that the probes are prepared by combinatory synthesis.

21. Method according to claim 20, further characterized in that different base structural units are labeled in such a way that the each of the probes synthesized from them can be distinguished by their mass in the mass spectrometer.

22. Method according to one of the preceding claims, further characterized in that the probes are prepared as sublibraries and these are provided with different mass and/or charge tags.

23. Method according to one of the preceding claims, further characterized in that matrix-assisted laser desorption/ionization mass spectrometry (MALDI) is conducted in f).

24. Kit for conducting the method according to claim 1, containing a sample holder for a mass spectrometer, which is modified in such a way that randomly selectable portions of a genome are immobilized on the latter, and/or probe libraries, with which the DNA immobilized on the sample holder is analyzed by mass spectrometer and/or other chemicals, solvents and/or adjuvants, as well as, optionally, instructions for use.